UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,171	06/20/2001	David Zarling	A-66914-2/RFT/NBC	8414

7590 10/01/2002

RICHARD F. TRECARTIN, ESQ.
FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
Suite 3400
Four Embarcadero Center
San Francisco, CA 94111-4187

EXAMINER
LOEB, BRONWEN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/01/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,171	ZARLING ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

DETAILED ACTION

This action is in response to the preliminary amendment filed 1 October 2001 in which claims 1-24 were amended and new claims 25-29 were presented.

Claims 1-29 are pending.

Drawings

1. The drawings are objected to because drawings appear to be missing. Specifically, the application was filed with two sheets of drawings comprising Figures 1, 2 and 5. The transmittal letter indicated four sheets of drawings were filed. The specification refers to Figures 1-6 (pp. 4-5). A Notice to File Missing Parts indicating the missing drawings was mailed 25 October 2001. Applicant's response to this notice, submitted 10 June 2002, did not provide the missing drawings. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

2. The disclosure is objected to because of the following informalities: The Brief Description of the Drawings refers to Figures 1-5 however only Figures 1, 2 and 5 were submitted. If Applicant does not submit the missing figures, all references to missing Figures 3, 4 and 6 should be deleted from the specification. Figure 5 should be renumbered Figure 3 and all references to it in the specification should be amended

accordingly. Since this application is a continuation of 09/373,347, missing Figures 3, 4 and 6 may be amended to the specification without the spectre of new matter if the figures submitted are identical to those in 09/373,347.

Appropriate correction is required.

Claim Objections

3. Claim 1 is objected to because of the following informalities: Claim 1 refers to "an amino acid sequence of interest" in the preamble but the method steps refer to "a polypeptide". It is suggested that the preamble be amended to recite "a polypeptide of interest" to provide consistency. Appropriate correction is required.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 5, 10, 15, and 18-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 9 of U.S.

Patent No. 6,074,853. "A pool of variant nucleic acids sequences of a pre-selected target nucleic acid sequence in an extrachromosomal sequence" is apparently identical in meaning and thus scope as "a library of altered nucleic acid sequences of a pre-selected target nucleic acid sequence in an extrachromosomal sequence". However the claims are not identical in scope because the definition of "substantially corresponds to" in the instant specification is broader than the definition in U. S. Patent No. 6,074,853. The narrower claims render obvious the broader claims in the pending application.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-29 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 5 are vague and indefinite in lacking a step that clearly relates back to the preamble. For instance, the step of claim 1 leads to the formation of a first library of altered target nucleic acids. The preamble however states "a method of domain specific gene evolution". The same is true for claim 3.

Claim 2 is vague and indefinite as it is unclear when this step takes place with respect to the first step recited in claim 1. Is the second library evolved from the first library (which is more clearly claimed in claim 25)? Or does the second library co-exist

with first library (ie. two separate libraries are generated?) Or is the second library evolved instead of the first library? For instance, is the second plurality added simultaneously with the first plurality such that in the method of claim 2, the "first library" of claim 1 doesn't ever get generated?

Claim 4 is vague and indefinite as it is unclear when this step takes place with respect to the first step recited in claim 3. Is the second library evolved from the first library (which is more clearly claimed in claim 26)? Or is the second pair of single-stranded targeting polynucleotides added simultaneously with the first pair such that the "first library" of claim 3 doesn't ever get generated? Or are two separate libraries generated from the same target nucleic acid sequence?

Claim 6 is vague and indefinite as it is unclear when this step takes place with respect to the first step recited in claim 5. Is the second library evolved from the first library (which is more clearly claimed in claim 27)? Or does the second library co-exist with first library (ie. two separate libraries are generated?) Or is the second library evolved instead of the first library? For instance, is the second plurality added simultaneously with the first plurality such that in the method of claim 6, the "first library" of claim 5 doesn't ever get generated?

Claim 8 is vague and indefinite as it is unclear when this step takes place with respect to the first step recited in claim 7. Is the second library evolved from the first library (which is more clearly claimed in claim 28)? Or does the second library co-exist with first library (ie. two separate libraries are generated?) Or is the second library evolved instead of the first library? For instance, is the second plurality added

simultaneously with the first plurality such that in the method of claim 8, the "first library" of claim 7 doesn't ever get generated?

Claims 10 and 11 are vague and indefinite in reciting "said library of altered target nucleic acids". With respect to claims 2, 4, 6, 8 and 25-28, it is unclear to which of the two recited libraries this phrase refers.

Claim 14 recites the limitation "said library of variant amino acid sequences" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim 23 recites the limitation "said target amino acid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 is vague and indefinite in claiming dependency on claims 7 and 8. In claims 7 and 8, the target nucleic acid is in a chromosomal sequence. Claim 24 recites that the target nucleic acid comprises an expression vector. So with respect to claims 7 and 8, is the method intended to evolve a chromosomally-integrated target?

Claim 29 recites the limitation "said recombination intermediate" in line 2. There is insufficient antecedent basis for this limitation in the claim with respect to claims 1, 2, 5-8, 25, 27 and 28.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the

> treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claims 1, 2, 5-14 and 16-29 are rejected under 35 U.S.C. §102(e) as being clearly anticipated by Pati et al (U.S.P. 5,948,653). Pati et al ('653) disclose a method of generating libraries of altered target nucleic acids comprising combining a target nucleic acid encoding a polypeptide of interest with a recombinase and at least one pair of single-stranded targeting polynucleotides having a homology clamp and wherein the targeting polynucleotides target a domain of a polypeptide of interest. Evolving two or more domains is taught. Targeting a complementary determining region is taught.Introducing libraries into cells to from a cellular library wherein the cell is either a prokaryotic cell or eukaryotic cell is taught. The target nucleic acid may be either in a chromosome or may be extrachromosomal. The recombinase may be either from a prokaryotic source or a eukaryotic source. The pairs of targeting polynucleotides may be coated with recombinase and may also comprise a chemical substitutuent. Selecting desired variants based on either the phenotype or desired activity is disclosed. Expressing the library of altered target nucleic acid sequences to generate a pool of variant polypeptide sequences is disclosed and the method wherein there is a plurality of amino acid substitutions is taught. See entire document, especially col. 19, line 31- col. 27, line 4, col. 27, line 38- col. 28, line 24, col. 28, line 65- col. 30, line 27 and col. 33, line 52-col. 35, line 57.

10. Claims 1, 2, 5-14 and 16-29 are rejected under 35 U.S.C. §102(e) as being clearly anticipated by Zarling et al (US 2002/0090361 A1). Zarling et al disclose a method of generating libraries of altered target nucleic acids comprising combining a target nucleic acid encoding a polypeptide of interest with a recombinase and at least one pair of single-stranded targeting polynucleotides having a homology clamp and wherein the targeting polynucleotides target a domain of a polypeptide of interest. Evolving two or more domains is taught. Targeting a complementary determining region is taught. Introducing libraries into cells to from a cellular library wherein the cell is either a prokaryotic cell or eukaryotic cell is taught. The target nucleic acid may be either in a chromosome or may be extrachromosomal. The recombinase may be either from a prokaryotic source or a eukaryotic source. The pairs of targeting polynucleotides may be coated with recombinase and may also comprise a chemical substitutuent. Selecting desired variants based on either the phenotype or desired activity is disclosed. Expressing the library of altered target nucleic acid sequences to generate a pool of variant polypeptide sequences is disclosed and the method wherein there is a plurality of amino acid substitutions is taught. See entire document, especially paragraphs 0072-0097, 0103-0110, 0114-0116 and 0124-0132.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to b patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

13. Claims 1, 2 and 5-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pati et al (U.S.P. 5,948,653). Pati et al ('653) is applied to claims 1, 2, 5-14 and 16-29 as above. Pati et al ('653) does not explicitly teach the method wherein the cellular library of expressed variant polypeptides sequences is secreted. At the time the invention was made, secretion of recombinant proteins was an obvious step to one of ordinary skill in the art. One would be motivated to do this because it hugely simplifies purification of the recombinant protein which is very desirable.

14. Claims 1, 2 and 5-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over Zarling et al. Zarling et al is applied to claims 1, 2, 5-14 and 16-29 as above. Zarling et al does not explicitly teach the method wherein the cellular library of expressed variant polypeptides sequences is secreted. At the time the invention was made, secretion of recombinant proteins was an obvious step to one of ordinary skill in

the art. One would be motivated to do this because it hugely simplifies purification of the recombinant protein which is very desirable.

15. Claims 1-14 and 16-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al as applied to claims 1, 2, 5-14 and 16-29 above, and further in view of Shortle et al (Proc. Natl. Acad. Sci. (1980) 77:5375-5379) and Stemmer (U.S.P. 5,605,793). Pati et al does not explicitly disclose contacting a recombination intermediate with a nuclease to form a nicked or open ended target nucleic acid and reassembling and recombining the target nucleic acid to produce a library of altered target nucleic acids; the method wherein it is recursive.

Shortle et al teach the use of single-strand specific S1 nuclease to nick the single-stranded DNA displaced in a recombinant intermediate formed by a recombinase, a target nucleic acid and a single-stranded targeting polynucleotide (see for instance p. 5375, Abstract). Stemmer teaches a recursive method of in vitro homologous recombination to form a library of altered nucleic acid sequences (col. 5, lines 59-63) wherein the target nucleic acid, to which polynucleotides having regions of homology and heterology with respect to the target nucleic acid sequence may be added, (col. 6, line 64-col. 6, line 3) is nicked by means of a nuclease (col. 7, lines 12-20), and is then reassembled and recombined to produce a library of altered target nucleic acids (col. 7, line 63- col. 8, line 45).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to combine method of recursive homologous recombination by Stemmer, the use of a single-stranded nuclease to nick the target nucleic acid as taught

by Shortle et al with the teachings of Pati et al to arrive at the method wherein a recombination intermediate is contacted with a nuclease to form a nicked or open ended target nucleic acid and reassembling and recombining the target nucleic acid to produce a library of altered target nucleic acids, and further wherein the method is recursive. One of ordinary skill in the art would be motivated to do this since the teachings of Shortle et al and Pati et al are directed to generating sequence alterations using recombinases, preferably RecA, and the formation of recombination intermediates, and Stemmer teaches a particularly advantageous way to utilize homologous recombination in generating sequence mutants.

16. Claims 1-14 and 16-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zarling et al as applied to claims 1, 2, 5-14 and 16-29 above, and further in view of Shortle et al (Proc. Natl. Acad. Sci. (1980) 77:5375-5379) and Stemmer (U.S.P. 5,605,793). Zarling et al does not explicitly disclose contacting a recombination intermediate with a nuclease to form a nicked or open ended target nucleic acid and reassembling and recombining the target nucleic acid to produce a library of altered target nucleic acids; the method wherein it is recursive.

Shortle et al teach the use of single-strand specific S1 nuclease to nick the single-stranded DNA displaced in a recombinant intermediate formed by a recombinase, a target nucleic acid and a single-stranded targeting polynucleotide (see for instance p. 5375, Abstract). Stemmer teaches a recursive method of in vitro homologous recombination to form a library of altered nucleic acid sequences (col. 5, lines 59-63) wherein the target nucleic acid, to which polynucleotides having regions of

homology and heterology with respect to the target nucleic acid sequence may be added, (col. 6, line 64-col. 6, line 3) is nicked by means of a nuclease (col. 7, lines 12-20), and is then reassembled and recombined to produce a library of altered target nucleic acids (col. 7, line 63- col. 8, line 45).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to combine method of recursive homologous recombination by Stemmer, the use of a single-stranded nuclease to nick the target nucleic acid as taught by Shortle et al with the teachings of Zarling et al to arrive at the method wherein a recombination intermediate is contacted with a nuclease to form a nicked or open ended target nucleic acid and reassembling and recombining the target nucleic acid to produce a library of altered target nucleic acids, and further wherein the method is recursive. One of ordinary skill in the art would be motivated to do this since the teachings of Shortle et al and Zarling et al are directed to generating sequence alterations using recombinases, preferably RecA, and the formation of recombination intermediates, and Stemmer teaches a particularly advantageous way to utilize homologous recombination in generating sequence mutants.

17. Claims 1, 2, 5-14, 16-22 and 24-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over Patten et al (USP 6,335,160 B1) in view of Zarling et al (USP 5,763,240). Patten et al teaches a recursive method of in vitro or in vivo homologous recombination to generate a library of variant nucleic acid sequences (col. 8, line 30-col. 14, line 23) and teaches targeting one or more protein domains (col. 12, lines 8-11 and col. 17, lines 1-7). Introducing the library into cells, either prokaryotic or eukaryotic, and

expressing it is taught. Using a plurality of targeting polynucleotides is also taught. Screening or selecting desired variants based on activity or phenotype is taught in col. 13, lines 37-45. Patten et al does not explicitly teach the use of pairs of targeting polynucleotides comprising homology clamps and a recombinase in their recursive method.

Zarling et al ('240) teach a method of generating a variant nucleic acid sequence of a pre-selected target nucleic acid sequence, particularly in a chromosomal sequence, wherein the altered sequence is generated by a recombinase, a target nucleic acid sequence and a pair of single-stranded targeting polynucleotides comprising homology clamps. Coating the targeting polynucleotides with recombinase is taught. The recombinase used may be either prokaryotic or eukaryotic. The use of chemical substituents is taught. See entire document, especially col. 9, line 55-col. 10, line 16, col. 10, line 41-col. 12, line 51, col. 13, lines 34-58 and col. 14, line 55- col. 16, line 16.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to combine the recombinase directed homologous recombination method of Zarling et al ('240) with the recursive method teachings of Stemmer. One of ordinary skill in the art would have been motivated to do so since Stemmer teaches the use of multiple methods of mutagenesis for use in his recursive evolution method (p. 10, lines 18-28) and both teach methods of mutagenesis using homologous recombination techniques.

Neither of these references explicitly teaches the method wherein the cellular library of expressed amino variant amino acid sequences is secreted. At the time the

invention was made, secretion of recombinant proteins was an obvious step to one of ordinary skill in the art. One would be motivated to do this because it hugely simplifies purification of the recombinant protein which is very desirable.

18. Claims 1-14, 16-22 and 24-29 are rejected under 35 U.S.C. §103(a) as being unpatentable over Patten et al in view of Zarling et al ('240) as applied to claims 1, 2, 5-14, 16-22 and 24-29, and further in view of Shortle et al and Stemmer. Patten et al and Zarling et al teach a method of domain specific gene evolution comprising combining a target nucleic acid sequence with a pair of single-stranded targeting polynucleotides having homology clamps and a recombinase, targeting one or more domains and performing the method recursively. Patten et al and Zarling et al do not explicitly teach the use of a nuclease to nick the recombination intermediate then reassembling and recombining the nicked target nucleic acid to produce a library of altered nucleic acid sequences.

Shortle et al teach the use of single-strand specific S1 nuclease to nick the single-stranded DNA displaced in a recombinant intermediate formed by a recombinase, a target nucleic acid and a single-stranded targeting polynucleotide (see for instance p. 5375, Abstract). Stemmer teaches a recursive method of in vitro homologous recombination to form a library of altered nucleic acid sequences (col. 5, lines 59-63) wherein the target nucleic acid, to which polynucleotides having regions of homology and heterology with respect to the target nucleic acid sequence may be added, (col. 6, line 64-col. 6, line 3) is nicked by means of a nuclease (col. 7, lines 12-

20), and is then reassembled and recombined to produce a library of altered target nucleic acids (col. 7, line 63- col. 8, line 45).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to combine the nicking of the recombination intermediate of Shortle and the reassembly and recombining method of Stemmer with the method taught by Patten and Zarling ('240). One of ordinary skill in the art would have been motivated to do so since both Stemmer and Patten et al teach the use of multiple methods of mutagenesis for use in recursive evolution methods (p. 10, lines 18-28) and all the references teach methods of mutagenesis using homologous recombination techniques.

Conclusion

Claims 1-29 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Customer service for Tech Center 1600 may be reached at (703)-308-0198.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

September 27, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of Attachment(s) 6). Other: Copy of Papers Originally Filed information.

09/886,171

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
10 June 2002	24 May 2002
7 August 2002	24 May 2002

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 12